

REMARKS / ARGUMENTS

Claims 1, 2 and 4-12 are pending in the application and stand rejected. By the foregoing amendment, the applicants have amended claims 1 and 12. No new matter is added by the amendments. Support for the amendments can be found in the specification as filed, for example on page 2. Applicants request consideration and entry of this amendment after final rejection. In view of the foregoing amendments and following discussion, the applicants submit that all pending claims are in condition for allowance.

On page 2 of the Office Action the Examiner rejected claim 12 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Claim 12 is amended. The language "0.16 percent" of amended claim 12 is supported on page 2 of the specification and thus is not new matter. Therefore amended claim 12 complies with the written description requirement and is allowable. Accordingly, the applicants request the Examiner withdraw the rejection.

On pages 3-8 the Examiner rejected claims 1-2, 4, 6 and 12 under 35 U.S.C. § 103(a) as being unpatentable over Adjei et al., (U.S. Pat. No. 6,261,539); over Lewis et al. (EP 1219293); and over Ashurst et al. (U.S. Pat. No. 6,511,652); and claims 1-2, 4 and 6 as being unpatentable over Keller et al. (U.S. Pat. 6,475,467). Claims 1 and 12 are amended. For the reasons discussed below, and those discussed in previous responses incorporated herein by reference, none of the references teach or suggest the claimed invention of amended claim 1. A showing that the claimed range achieves unexpected results relative to the prior art range rebuts a *prima facie* case of obviousness based on claimed ranges that overlap or lie inside ranges disclosed by the prior art. *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). None of the references teach or suggest the superiority of the claimed range of water of amended claim 1 to result in a significantly better single actuation reproducibility (SAR) for "cans" containing albuterol sulfate and ipratropium bromide with a water content of 1300 to 1800 ppm to release the same amount of albuterol sulfate (*i.e.*, % of theory) during each single actuation event. None of these references would lead a skilled artisan to conclude the claimed range of water content would have a significant effect on the SAR.

The Examiner did not find persuasive the previously made arguments alleging that: (1) standard deviation is not a support for unexpected result and that standard deviation does not show patentability distinction (page 14 of the Office Action); (2) in a formulation the criticality

is its function as a formulation and unexpected results show unexpected bioavailability of the formulation, and that a showing of consistency of spraying is not support for bioavailability (page 15 of the Office Action); (3) the claimed range of “about 0.13%” reads on 0.12% which Declaration considers poor reproducibility (page 15 of the Office Action); and (4) although Adjei, Lewis and Ashurst do not teach the specific claimed range, the disclosed ranges of the prior art references meet the claimed range and they all recognize that a small amount of water is advantageous in stability of the formulation and the reproducibility of the actuations (page 15 of the Office Action). The applicants address each allegation below.

The applicants submit the Examiner is incorrect as to allegation (1). MPEP § 716.02(b)(I) states the “evidence relied upon should establish ‘that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance’”. In this particular instance, the distribution of the data points (i.e., each actuation event) and the width of the curve reflect unexpected and unobvious results of both statistical and practical significance. The applicants submit the standard deviation is supportive of the unexpected result and a patentable distinction. Therefore the data provided in the Declaration of George DeStefano (“DeStefano Declaration”) shows the claimed water content of amended claim 1 provides unexpected superior results in the reproducibility of actuation events.

As to allegation (2), the applicants disagree. Firstly, the Examiner has not provided any support for the criticality of formulations to pertain only to unexpected bioavailability. Secondly, there is no basis for concluding improved consistency in activator events is not a critical function of a formulation. Rather, a skilled artisan would conclude that consistency of activator events is an important factor in obtaining consistent bioavailability. Thus, consistency of activator events is critical to a formulation.

As to allegation (3), the applicants have amended claim 1. Amended claim 1 reflects the range of water content resulting in unexpected superior results in reproducibility of actuation events.

As to allegation (4), the applicants disagree. The applicants submit that a small amount of water (ranging from 0.0 to 5.0% in the prior art references) is very different than a small specific percentage range of water. A skilled artisan viewing the water content ranges of the prior art references would not contemplate a specific percentage range of water content, especially those which have unexpectedly superior properties over other percentages.

Furthermore, none of the references disclose that water is advantageous in reproducibility of actuations. Adjei merely discloses water above nascent levels aid as a stabilizer to the medicinal aerosol formation (col. 2 and col. 3), Ashurst does not indicate the addition of water is advantageous, and Lewis discloses that a small amount of water may be added to improve the solution of the active material (paragraph [0063]). Therefore, none of Adjei, Lewis and Ashurst teach or suggest the claimed water content of amended claim 1 resulting in unexpected superior properties.

In light of the above discussion, the data presented in the DeStefano Declaration clearly illustrates the unexpected superiority of the claimed water content in the reproducibility of actuation events. One skilled in the art viewing any one of Adjei, Ashurst, Lewis or Keller would not expect that water content as claimed would have such a profound effect on actuation reproducibility. Water content is not identified in any of the prior art references as an important factor for this characteristic. One skilled in the art would be led to believe water content is not an important factor in achieving reproducibility. Thus, amended claim 1 is not obvious in light of the prior art references. Claims 2, 4, 6 and 12 which depend from amended claim 1 are also not obvious and are therefore allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejections.

On pages 9-11 the Examiner rejected claims 5 and 7-11 under 35 U.S.C. § 103(a) as being unpatentable over Adjei et al. in view of Jager et al. (WO 9413262); and as being unpatentable over Lewis et al. in view of Jager et al. (WO 9413262). For reasons similar to those discussed above, and those discussed in previous responses incorporated herein by reference, the combination of the references does not result in the claimed invention. Neither Adjei alone or in combination with Jager nor Lewis alone or in combination with Jager teach or suggest the claimed water content of amended claim 1 that results in unexpected actuation reproducibility. Since the combinations of Adjei and Jager as well as Lewis and Jager do not result in amended claim 1, dependent claims 5 and 7-11 cannot be obvious over Adjei in view of Jager or Lewis in view of Jager and are thus allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejections.

On page 12 the Examiner rejected claims 1-2, 4-12 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Pat. No. 6,423,298 in view of Adjei et al. The applicants respectfully traverse the rejection. For reasons

similar to those discussed above, and those discussed in previous responses incorporated herein by reference, amended claim 1 is not obvious over the combination of the references. The combination of the references cannot teach a skilled artisan the claimed water content that results in unexpected actuation reproducibility as discussed above. Therefore, the combination of the '298 patent and Adjei does not result in the claimed invention. Thus, claims 1, 2 and 4-12 are not obvious over the '298 patent in view of Adjei and are therefore allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejection.

Applicants submit that all claims pending in the patent application are in condition for allowance. Accordingly, entry of this amendment, reconsideration of this application and its swift passage to issuance are earnestly solicited. In the event there are any fees due and owing in connection with this matter, please charge same to our Deposit Account No. 11-0223.

Respectfully submitted,

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